American Journal of Hematology 63:42–45 (2000)

Choroidal Infiltrates Simulating Fundal Changes of Acute Leukemia During Hematological Recovery Following High-Dose Chemotherapy in Acute Myelomonocytic Leukemia in Remission

Kanjaksha Ghosh,* Sandip Mitra, and Devendra Hiwase
Sultan Qaboos University Hospital, Muscat, Sultanate of Oman

A young female patient of 18 who was diagnosed to have acute myelomonocytic leukemia (AML M4) developed choroidal infiltrate and fundal changes suggestive of acute leukemia deposits while she was in remission and was recovering from chemotherapy induced myelosuppression. The choroidal infiltrates were associated with peripheral blood and CSF monocytosis. The choroidal lesion resolved on its own in 2 week's time, when the peripheral and CSF monocytosis subsided. Interestingly this patient had pseudo-Chediak Higashi inclusions in leukemic blasts with normal karyotype. Am. J. Hematol. 63:42–45, 2000. © 2000 Wiley-Liss, Inc.

Key words: choroidal infiltrates; retinal hemorrhages; fluorescein angiography; myeloblast; pseudo-Chediak Higashi inclusions

INTRODUCTION

Changes in the optic fundi are discernable in a large proportion of patients with acute and chronic leukemia [1–4]. Every ocular structure is known to be involved in this group of disease [1], and it was often the ophthalmologist who used to suggest the diagnosis of leukemia when laboratory medicine was in its infancy and marrow study was infrequent [5].

However, many of the changes in the ocular fundi are nonspecific and are really not the sine qua non of the leukemic process. We describe here an unusual case of sudden visual loss with retinal hemorrhages, choroidal nodules, and widespread changes in fluorescein angiography, suggesting the diagnosis of acute leukemia, but in reality the patient was in remission and was recovering from her third consolidation chemotherapy. These changes were associated with low platelet counts, peripheral blood, and central nervous system monocytosis. All changes of leukemic retinopathy subsided over the course of 14 days without any intervention, when the blood and CNS monocytosis subsided. We believe the changes were due to a combination of monocytic infiltration of ocular structure with associated thrombocytopenia.

CASE REPORT

An eighteen-year old married female presented with cervical lymphadenopathy, gross enlargement of tonsils, gingivial hyperplasia, and a 5-cm enlarged liver and spleen. She also had a diffuse indurated and tender lump in the left breast and severe halitosis. She had no bleeding manifestation, and she was found to be moderately pale. Examination of ocular fundi at that time showed pallor but no hemorrhage or papilloedema. As she was breast-feeding her six-month old son, the indurated tender breast lump was thought to be an evolving breast abscess. Peripheral blood examination showed hemoglobin of 9.4 g/dl, WBC 6.8×10^9/l, platelets 365×10^9/l, and peripheral smear showed 33% monocytosis and 18% blasts with myeloid morphology; 5–10% of the blasts contain giant pseudo-Chediak Higashi granules (Fig. 1). Bone marrow aspirate confirmed the diagnosis of acute myelomonocytic leukemia with blast cells (18–25%)

*Correspondence to: Dr. Kanjaksha Ghosh, MD, MRCP.MRCPath. MRCPI.MNAMS, Institute of Immunohaematology, 13th floor, KEM Hospital MS building, Mumbai 12, Parel 400012, India.

Received for publication 16 July 1999; Accepted 1 September 1999

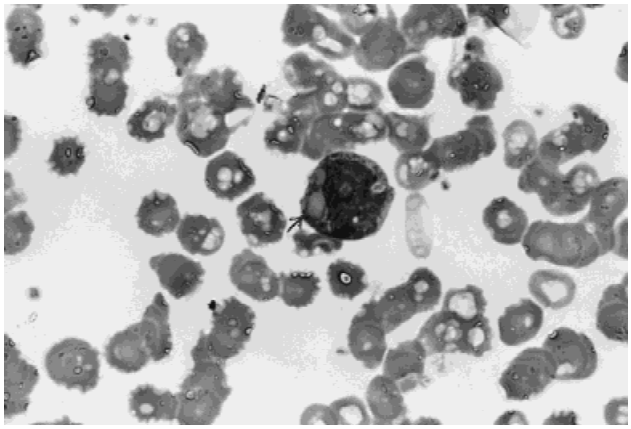

Fig. 1. Myeloblast in peripheral smear showing giant inclusions (400×).

showing giant pseudo-Chediak Higashi granules similar to peripheral smear. A G-banded karyotype from bone marrow aspirate showed normal 46 XX chromosomes. The patient was put on combination of metronidazole along with pipercillin and gentamicin intravenously. Oral Cabergoline was started to stop breast milk. She was started on combination chemotherapy with Daunorubicin and cytosine arabinoside. Following the first course she went into remission. However, during the recovery phase, blood counts she showed significant monocytosis (6.2×10^9/l) with features of consolidation of the lung and left-sided pleural effusion. She improved with resolution of lung lesions and pleural effusion with normalization of peripheral blood counts. The cytology of the plural effusion showed a large number of active vacuolated monocytic cells. Her breast lump subsided on combination of Carbergoline and intravenous antibiotic therapy.

Subsequently she received three courses of consolidation therapy during the recovery from cytopenia; during each course of therapy, she had significant monocytosis ($2.5–7.2 \times 10^9$/l), tender hepatomegaly with normal echo pattern, lobar consolidation with plural effusion, and sudden loss of vision. During recovery from the third consolidation therapy with high dose Ara C and Mitoxantrone, she developed sudden diminution of vision without any headache. At that time her platelet count was 12×10^9/l and peripheral monocyte count 2.8×10^9/l with absolute neutrophil count 0.1×10^9/L and hemoglobin of 8.9 g/dl. A lumbar puncture done at the same time showed monocytosis with large number of vacuoles in it (Fig. 2). Her vision in the right eye dropped to 6/60, and in the left eye it dropped to 6/36.

Fundus photography showed yellowish white choroidal deposits at the fovea centralis with macular haemorrhage in the right eye (Fig. 3) but the left eye showed preretinal haemorrhage at the macula 2 disc diameter temporal to fovea centralis with yellowish white choroidal infiltration with fuzzy margins and surrounding retinal oedema (Fig. 4).

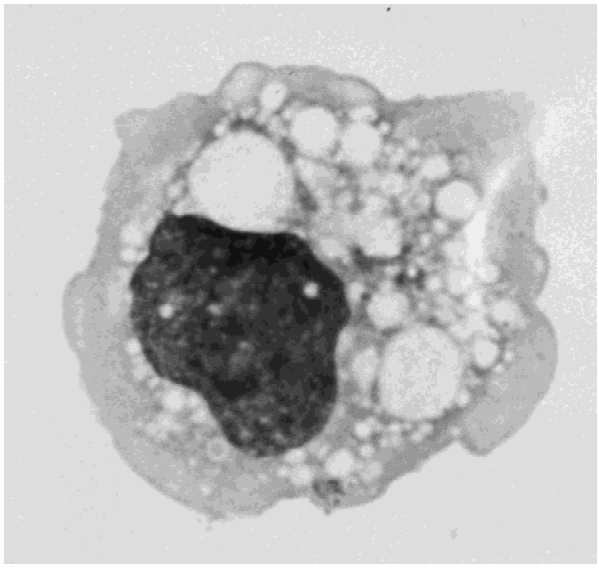

Fig. 2. Monocyte with large number of vacuoles from the cerebrospinal fluid of the patient (1500×).

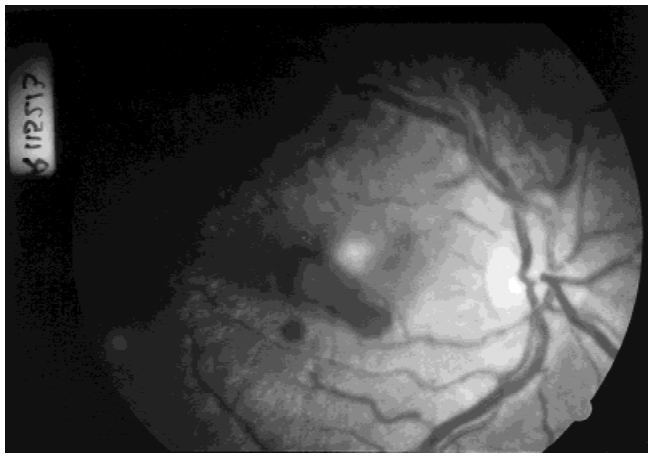

Fig. 3. Right eye fundus picture shows yellowish white choroidal deposits at the fovea centralis with macular hemorrhage.

Fluorescence angiography showed hypofluorescence corresponding to the area of choroidal infiltration with hyperfluorescent border corresponding to retinal oedema and late leakage from optic disc, suggestive of optic disc oedema. Blocked areas of fluorescence corresponded to the area of haemorrhage (Figs. 5 and 6).

Two weeks later when the patient's visual acuity improved in both eyes to 6/9 fundal photography showed absorbing haemorrhage and resolving choriodal infiltrates (Figs. 7 and 8).

Presently the patient has normal visual acuity with

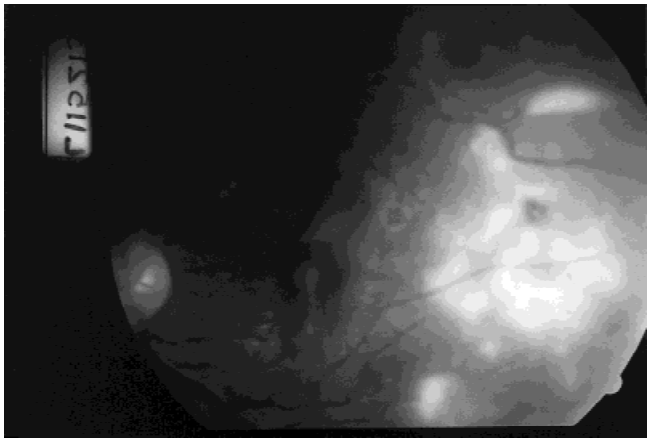

Fig. 4. Left eye fundus picture shows, preretinal hemorrhage at the macula, superficial hemorrhages with whitish centre along the inferotemporal arcade, and 2 disc diameter temporal to the fovea centralis, shows yellowish white choroidal infiltration with fuzzy margins and surrounding retinal oedema.

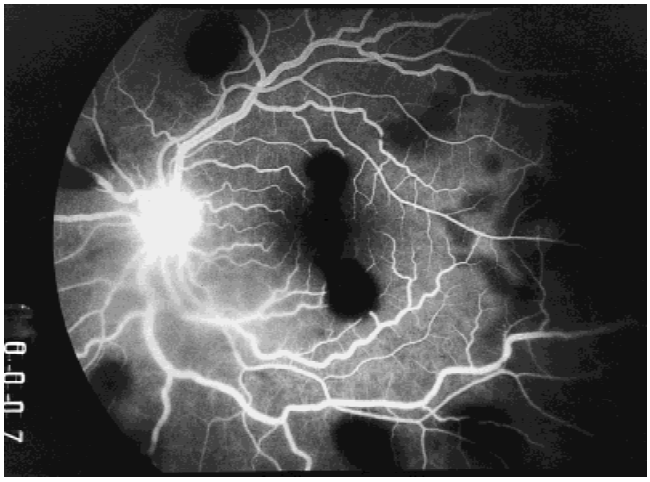

Fig. 5. Fundus fluorescein angiography of the left eye shows hypofluorescence corresponding to the area of choroidal infiltration and hyperfluorescent border corresponding to the retinal oedema and late leakage from the optic disc, suggestive of optic disc oedema. There are blocked fluorescence corresponding to the hemorrhages.

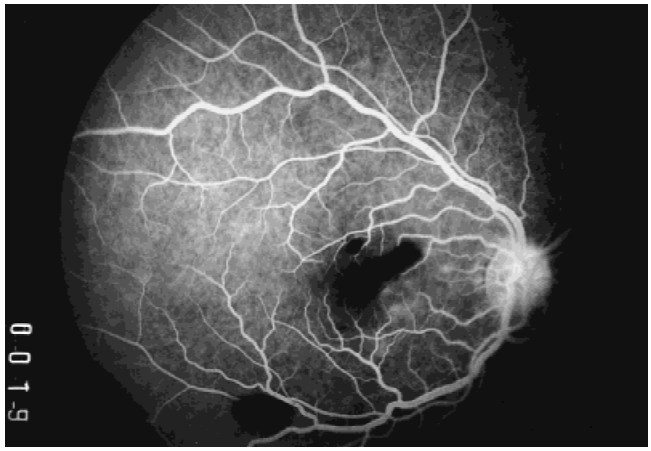

Fig. 6. Fundus fluorescein angiography of the right eye shows blocked fluorescence corresponding to the hemorrhages.

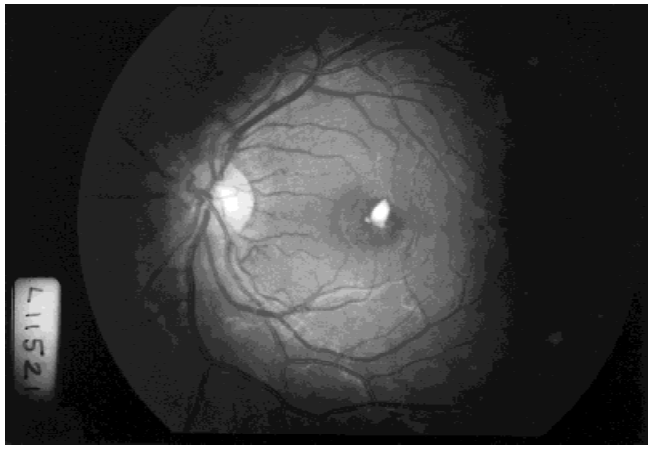

Fig. 7. Fundus pictures of the left eye shows yellowish white remnants of the absorbing retinal hemorrhage at the fovea centralis and evidence of healed choroiditis to the macula.

no evidence of any deposit she continues to be in marrow remission.

DISCUSSION

This patient present several interesting and rare clinical observations. Generally acute myeloid leukemias do not present with cervical lymphadenopathy and grossly enlarged tonsils [6] though monocytic and mylomonocytic leukemias may present with tissue infiltrations like liver, spleen, skin, gums, and retina. Pseudo-Chediak Higashi granules in acute myelomonocytic leukemias have been reported in several cases reports [7,8] in the late 1970s and early 1980s, but apart from the morphological oddity nothing much is known about the biology of this variety of AML. Recently, a case of AML-M3 was reported with this anomaly [9]. To today, only 35 such cases has been reported in the world literature, including 16 patients from pediatric age group. In none of these patients retinal changes have been reported. Fundus changes have been studied systematically in large number of acute myeloid leukemias [1] and in one-third of such patients no ocular abnormalities were present at the time of presentation, and the commonest abnormalities were in the form of various retinal changes like cotton wool spots, hemorrhages, and various retinovascular abnormalities.

One of the striking features in the present case was the development of choroidal infiltration and retinovascular

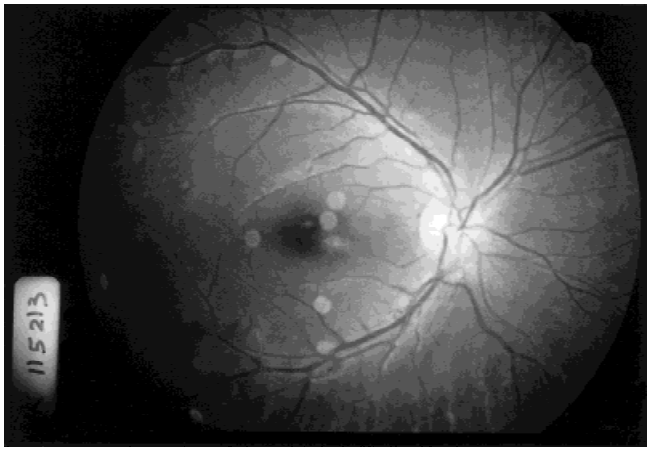

Fig. 8. Fundus picture of the right eye shows yellowish white remnant of the absorbing retinal hemorrhage.

abnormalities when the patient was in remission and was recovering from chemotherapy-induced cytopenia. As during the time of sudden visual deterioration, her platelet counts was only 12×10^9/l retinal hemorrhages could be explained by thrombocytopenia [4]. However, the choroidal infiltrates may be explained by monocytic infiltration as this patient had shown similar infiltrate pathology of the lung and possibly of liver during recovery from chemotherapy-induced pancytopenia heralded by brisk monocytosis though she was not receiving any growth factor. Moreover, the choroidal infiltrates were also associated with CSF and peripheral blood monocytosis. The resolution of the lesion over 2 weeks happened without any additional therapeutic intervention with normalization of the peripheral blood picture.

REFERENCES

1. Karesh JW, Goldman EJ, Reck K, Kelman E, Schiffer CA. Prospective ophthalmic evaluation of patients with acute myeloid leukemia: correlation of ocular hematological findings. J Clin Oncolog 1989;7(10): 1528–1532.
2. Gupta A, Jain IS, Verma S, Ghosh K, Pandav SS. Papilloedema in chronic myeloid leukemia. Bull P G I 1987;21:15–19.
3. Allen RA, Staatsma BR. Ocular involvement in leukemia and allied disorders. Arch Ophthalmol 1961;66:68–86.
4. Holt JM, Gordon Smith EC. Retinal abnormalities in the diseases of the blood. Br J Ophthalmol 1969;53:145–160.
5. Culler AM. Fundus changes in leukemia. Trans Am Ophthalmol Soc 1951;49:445–473.
6. Lichtman MA. Acute myelogenic leukemia. In: Beutler E, Lichtman MA, Coller BS, Kipps TJ, William's Haematology, editors. 5th edition. New York: McGraw Hill, Inc., 1995. p 172–298.
7. Van Slyck EJ, Rebuck JW. Pseudo-Chediak Higashi anomaly in acute leukemia. A significant morphologic corollary. Am J Clin Pathol 1974; 62:673–678.
8. Dittman WA, Kramer RJ, Bainton DF. Electron microscopic and peroxidase cytochemical analysis of pink pseudo-Chediak Higashi granules in acute myelogenous leukemia. Cancer Res 1980;40:4473–4481.
9. Symes PH, Williams ME, Flessat C, Srivastava AK, Swerdlow SH. Acute promyelocytic leukemia with pseudo-Chediak Higashi anomaly and molecular documentation of t(15;17) chromosomal translocation. Am J Clin Pathol 1993;99:622–627.